ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

1959

243 CHARLES STREET

BOSTON, MASSACHUSETTS

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Richard F. Brubaker: *Clerkship*

The aim of the Howe Laboratory is to integrate clinical ophthalmology and the basic sciences through research, teaching, and contact with patients. This requires a team of persons having varied backgrounds and talents. It also requires enthusiasm, persistence, and other less obvious qualifications. But training, talents, enthusiasm, and all the other intangible attributes would amount to little more than a dream were it not for the loyal and generous benefactors that provide the subsidy. All of us, investigators and benefactors alike, have contributed in his or her own way to the work that is reported herein.

Research Activities

Ocular Hydrodynamics and Glaucoma. Experimental studies in the laboratory by Dr. Grant have been directed toward explaining certain clinical abnormalities of the intraocular pressure.

At the time of the last Report, perfusion experiments had shown that 75 per cent of the resistance to drainage out of the normal human eye occurred at the trabecular meshwork. Analogous observations on three eyes with open angle glaucoma have now indicated that glaucomatous obstruction is due to increased resistance in this trabecular meshwork. This obstruction, although often hypothecated as the site of abnormality in glaucoma, has not previously been verified by direct measurement.

Distortion or displacement of the ciliary body has been found to influence the hydrodynamics of the eye. In describing artificial narrowing of the anterior chamber, it was suggested in last year's Report that the forward displacement of the ciliary body might be significant in several clinical conditions. A correlation of Dr. Grant's experiments with clinical observations of Drs. P. A. Chandler and A. E. Maumenee points to a distortion of the ciliary body in the following: (1) separation of the choroid (which often follows ocular surgery); (2) scleral buckling procedures; (3) congenital glaucoma; and probably (4) malignant glaucoma. When analogous distortion of the ciliary body and separation of the choroid have been induced in enucleated human eyes by injection of fluid between the sclera and choroid, the outflow may be jeopardized. Were this not compensated for by reduction in aqueous humor formation, glaucoma would certainly ensue. Incidentally it has been

found that there are no outflow channels in the enucleated eye from the perichoroidal space such as there are from the anterior chamber.

The facility of outflow in the enucleated eye has not been significantly altered by collagenase and alpha chymotrypsin. On the other hand, hyaluronidase, previously found to be ineffective on eyes removed post-mortem, was found to increase the outflow in eyes enucleated in vivo.

Noteworthy are several other studies aimed at a clarification of intraocular fluid dynamics. Yttrium chloride and lanthanum chloride have been found to be suitable fixatives for histologic study of the meshwork since they do not decrease the outflow whereas formaldehyde, glyoxal, glutaraldehyde, osmic acid, and lead acetate were unsatisfactory. The Goldman Aplanation Tonometer has been modified by Dr. Grant and Mr. Mueller to permit measurement of intraocular pressure in recumbent patients. This arrangement is particularly applicable for determination of scleral rigidity and for measurement of the pressure in infants' eyes. Finally, preliminary study of the dynamic elastic properties of the eye with the aid of an analog computer reveals a complexity greater than indicated by former methods.

Histochemistry. Since enzymes control most of the metabolic processes in the body, a knowledge of their distribution is of paramount importance. The retina of the eye lends itself particularly well to a study of certain enzymes concerned with energy production, and an extensive study of this tissue has therefore been carried out over the past two years by Drs. Kuwabara and Cogan. The result has been a map of the distribution of many of the enzymes that make energy available to the retina. These findings, which are of great interest histochemically, should provide a valuable guide to the study of retinal disease and are currently being reported in a series of articles in the *Journal of Histochemistory and Cytochemistry*. The observations will shortly be extended to ocular tissue other than the retina. It is especially hoped to chart out the distribution of some of the enzymes in membranes concerned with intraocular fluid formation and other functions essential to the eye.

Another aspect of histochemistry which has been recurrently noted in these Annual Reports is that pertaining to cystinosis. This tragic disease, seen almost exclusively in children, is an inborn error of metabolism. It has unusual ophthalmologic significance because of the characteristic deposits of crystals in the cornea and conjunctiva by which the diagnosis may be made. Although the conjunctival crystals have been studied in biopsy material by numerous investigators, including ourselves, the corneal crystals have probably never been seen heretofore in histologic material. The opportunity to make such a study in detail presented itself this past year. To our surprise the corneal crystals, in contrast to those occurring elsewhere in the body, were most elusive. Moreover, they had a needle shape unlike those found in other tissues. We have as yet not explained this latter feature but we were able to establish that they were cystine and not tyrosine as their morphology might suggest.

We also had the privilege of participating in a project this past year with the Pathology Departments of the Children's Medical Center and Massachusetts General Hospital leading to a demonstration for the first time of cystine crystals in the white blood cells of children with cystinosis.

In addition to the foregoing histochemical studies on cystinosis of children, a study was made on degenerative changes in the eyes of people at the other end of the age scale. A common occurrence in senescence is the development of focal areas of scleral translucency just in front of the tendinous insertions of the medial and lateral rectus muscles. A few years ago we found by chance that one of these areas contained a plaque of calcium sulfate (gypsum). This seemed of unusual interest because such a form of calcification had never been previously reported in biologic tissue. Since this initial observation, we have studied other cases of focal scleral translucency that have become available to us through the facilities of the BostonEye Bank. We still do not understand how these foci become transparent or why they localize in front of the rectus tendons but we can report that the histologic changes consist primarily of a loss of cellularity. The calcification is a secondary and late occurrence. Although the calcific plaque in the case originally studied was almost entirely in the form of calcium sulfate, the plaques in three subsequent cases subjected to crystallography

were calcium phosphate with only a minor component, in one case, of sulfate.

Biochemistry. In keeping with the modern trends in research, a considerable part of the Howe Laboratory is devoted to biochemistry. This section is directed by Dr. Jin Kinoshita and its activities of the past year have centered about certain aspects of lens and retinal metabolism.

Much of the work on the lens is aimed at elucidating the abnormal processes involved in cataract formation. Since the time of Morner (1894) the lens has been thought to contain three different proteins. It now seems that these represent three major classes of proteins rather than individual proteins. By means of chromatography on a modified cellulose column, Dr. Spector has been able to fractionate calf lens proteins into ten separate components. With this separation into individual lens proteins it is now possible to study their individual properties, their synthesis, and, possibly, the changes which take place in them or in their counterparts from human lenses when cataracts occur.

Electrolyte studies of the calf lens have indicated how dependent the lens is on its environmental fluid. The calcium ion concentration is particularly important in maintaining the normal levels of potassium and sodium in the lens. Normally, the lens has the high potassium-low sodium distribution characteristic of intracellular components but a slight drop in the calcium of the bathing medium causes a decrease in the potassium and increase in the sodium. It appears from these studies that the calcium concentration of the environmental fluid must be maintained at a certain critical level in order to maintain the normal permeability properties of the lens. The obvious application of these findings is in the case of hypoparathyroid cataracts where a lowered calcium in the aqueous humor is associated with the development of cataracts.

Glucose metabolism is another factor which was found to be important in maintaining the normal cation composition in the lens. In progress are experiments on the alteration of glucose utilization by the cataractous lens in experimental diabetes.

Biochemical studies on the retina, begun by Dr. Sidney Futterman under the auspices of the Retrolental Fibroplasia

Project, are being continued by him in the Howe Laboratory. The mitochondria of cattle retina, isolated by high speed centrifugation, are being studied in order to elucidate one of the major metabolic pathways in retinal tissue. Retinal mitochondria have been found to differ in some of their properties from mitochondria prepared from other tissues. The enzyme lactic dehydrogenase was found in cattle retina to be composed of five similar but separable protein components while the corresponding enzyme in the cornea was composed of only three components. The kinetic properties of these components which have been studied include the reactions of the enzyme with reduced cofactors and the pH dependence of the enzymatic activity.

Biochemical investigations of a different nature have been aimed at determining the metabolic basis for corneal opacification and partial blindness in a group of children with a particular hereditary disease of the eye. This entity, which has not been well defined clinically and in consequence has not been named, consists of a diffuse opalescence of the corneas similar to that which occurs in a disease variously called lipochondrodystrophy or Hurler's disease. Unlike this latter disease, however, the patients under study have not had the dwarfism and other features characteristic of lipochondrodystrophy. This past year Mr. Richard Brubaker, a medical student at the Harvard Medical School, investigated with Dr. Kern the mucopolysaccharide excretion in the patients with this corneal disease and in patients with lipochondrodystrophy. The results again suggest a basically different metabolic defect in the two diseases.

Toxicology and the Cornea. The chemical reactions induced in the cornea by various poisons have been partially concerned with the interaction of various metals, organic acids, and bases with the cornea. As the work of Drs. Grant and Kern progressed, it has become apparent that more information is needed on the interaction of the cornea with chemicals that are normally present and not toxic to the cornea. Accordingly, the relevant work of the past year has stressed the interaction of sodium chloride with the cornea and with the collagen and mucoproteins of the cornea.

A comparison of purified collagen and whole cornea has brought to light a fundamental difference in the reactivity of

these two tissues. Collagen preferentially attracts anions, such as chloride, whereas the cornea as a whole preferentially attracts cations, such as sodium. Yet the forces of either collagen or cornea binding these physiologic ions is less than that which will bind toxic ions. It appears that many of the supposedly free acidic and basic groups of the normal tissue are neutralizing each other by salt linkage and are therefore unavailable for attracting sodium and chlorine ions.

Physiology. Various studies are being made by Dr. Kupfer to gauge the formation of aqueous humor. Attempts to maintain the production of this fluid by electrochemical means have not yet been satisfactorily adapted to the rabbit eye. However, polyethylene tubes implanted into the anterior chamber of rabbit eyes, have permitted prolonged measurements of the flow of aqueous humor through these artificial channels.

The electric potential across the cornea of the living rabbit is being studied by Dr. Kupfer and Dr. Ephraim Friedman of the Infirmary's Resident staff. An attempt is being made to determine what the significance of this potential is for the maintenance of corneal deturgescence in terms of a sodium or water pump.

In a conjoint investigation with Dr. Kuwabara, Dr. Kupfer has been studying the distribution of motor end plates in human extraocular muscles. By means of the histochemical localization of cholinesterase it has been found that these muscles, unlike those of most skeletal muscles, have several nerve endings for each muscle fiber. Anatomic evidence is also being accumulated that may bear on the unsettled question of proprioception in these muscles.

A series of goniophotographs is being collected by Drs. Kupfer and Donaldson that will illustrate the development of the angle meshwork in fetal and early life. These will be correlated with the anatomic structures seen in microscopic cross sections of the same eyes. This study should provide important data for the understanding of congenital abnormalities which occur in this area and result in glaucoma.

To determine whether or not abnormalities in color vision may provide significant leads in the interpretation of neurologic lesions, Dr. Donaldson has constructed an apparatus to test

color sensations in response to moving black and white objects. This is being evaluated now on normal persons and if practicable it will be used in conjunction with the neuro-ophthalmic evaluation of patients with brain disease.

Lipid Studies. A major interest of the Laboratory continues to center about the use of the eye as an indicator of pathologic fat metabolism in the body. No detailed account will be given this year, however, since much of the activity in this area has been the consolidation of observations previously outlined and the exploration of new leads which are as yet only in a preliminary stage. However, it may be noted that Dr. Andrews has set up micromethods for lipid analysis by silicic acid chromatography and for fatty acid separation by gas chromatography. These techniques are being applied to the identification of the fatty components in such conditions as aberrant lipogenesis, arcus senilis, and atheromatous plaques.

Instrumentation and Optics. A new apparatus and technique for charting visual fields is under development by Dr. Donaldson. One of the major difficulties of previous techniques has been the monitoring of a patient's fixation. To lessen this difficulty the new apparatus incorporates an ingenious sound mechanism which will register any loss of fixation. This is to be used, in the first model at least, in conjunction with a large (5 foot) hemisphere on which both central and peripheral fields will be tested. Since the apparatus has yet to be evaluated under clinical conditions it would be premature to venture an estimate of its feasibility or ultimate value. Under laboratory conditions it does seem promising.

The stereoscopic camera for fundus photography has now reached a reasonably definitive state of development. After several years of trial and redesign, Dr. Donaldson has built a camera that is yielding most satisfactory results. The ease of focussing and the depth and clarity of the resultant photographs are superior to those obtained with any other available method. It is now planned to make a collection of fundus photographs of various clinical conditions. This will supplement the large collection of photographs of external conditions which Dr. Donaldson has accumulated over the past ten years.

Another problem involving instrumentation is the use of a split ocular for measurement of corneal thickness. This has

been found to be useful in various clinical conditions but is especially valuable for conditions in which opacification of the cornea prevents the use of other types of apparatus.

Neuro-ophthalmology. Activity in this subspecialty, which has for years been a conspicuous interest in the Howe Laboratory, was intensified for a part of this past year by the assignment of Drs. J. Lawton Smith, a National Institutes of Health Fellow, and Andrew Gay, a Heed Fellow, to this field. The specific studies carried out were: a statistical evaluation of inter-nuclear ophthalmoplegia with emphasis on the differentiation of the unilateral and bilateral types; the topical significance of the opticokinetic response in brain disease; the topical significance of spasticity of conjugate gaze in brain disease; and the value of a posture test in measurements of the retinal blood pressures in patients with cerebrovascular insufficiency. Reports were also prepared on such rare entities as see-saw nystagmus with suprasellar tumors, convergence nystagmus with lesions in the pineal region, and conjunctival teleangectasia in association with degeneration of the cerebellum. Finally, monthly staff conferences were organized for the presentation of neuro-ophthalmic problems and a week-long course on neuro-ophthalmology was conducted by Drs. Cogan, Donaldson, Smith and Gay.

While having no official connection with the Howe Laboratory, it may be noted that a considerable expansion in the neurophysiologic aspects of vision have occurred at the Harvard Medical School this past year with the appointment of Dr. Stephen Kuffler to the faculty. It is hoped that we may bridge the gap between the fundamental studies of Dr. Kuffler's group and our clinical problems. We have already begun, through Dr. Carl Kupfer, collecting material that may help correlate the visual field defects with lesions in the retina, optic nerve and tracts, and the lateral geniculate bodies.

All in all, it has been a very active year neuro-ophthalmologically and again underscored the favorable environment and challenging opportunities that exist in the relationships of the Laboratory with the Department of Neurology at the Massachusetts General Hospital and with the clinics of the Massachusetts Eye and Ear Infirmary.

Miscellaneous. The extraordinary observation that human vitreous humor had antibacterial properties was recently reported in the ophthalmic literature. To test this and determine the basis for it, Dr. Kevin Hill, now a Resident on the Infirmary Staff, studied the vitreous removed from eyes obtained through the Boston Eye Bank. Instead of using pooled samples of vitreous as had been the practice previously, Dr. Hill tested the antibacterial properties of individual samples (against the bacteria, staphylococcus aureus and pseudomonas aeruginosa). Interestingly only certain cases showed antibacterial properties and when the results were correlated with the clinical histories, it was found that only those samples were antibacterial which had come from donors receiving antibiotics at the time of death. In other words, the alleged antibacterial properties of human vitreous was in fact due to the presence of antibiotics which had come into the vitreous. Moreover, this effect could be negated by the addition of penicillinase to the vitreous samples from persons who had been receiving penicillin.

The possibility of settling the age-old question on the survival or replacement of donor cells in corneal grafts is being looked into in view of recent developments in chromosone tagging. Dr. Sweebe, who is spending two or more post-residency years at the Infirmary, is doing the experimental transplants on animals while Dr. Kuwabara will supervise the histologic studies.

Studies on the biology and thereapy of toxoplasmic infections of the eye are being continued by Dr. Kaufman during his residency. Dr. Kaufman has returned to the Infirmary after two years' training at the National Institutes of Health where his prime interest was toxoplasmosis. His present studies are concerned with the refractoriness of different strains of the toxoplasma organisms to pyrimethamine (Daraprim) and to the sulfa drugs. He will also serve as a consultant for many of the clinical cases of uveitis where toxoplasmosis and virus diseases are thought to be the cause.

Service Activities

Along with the research that has been sketched in the foregoing paragraphs, activities of a service nature have been allied functions of the Laboratory. The staff has participated at

various levels of teaching. At the undergraduate level, the Laboratory group conducted lectures in physiology (Dr. Kupfer), pharmacology (Dr. Grant), and pathology (Dr. Cogan). At the postgraduate level various members of the Laboratory gave an integrated course on ophthalmic biochemistry (Drs. Kinoshita, Kern, Futterman, Spector, Kuwabara, and Cogan), on neuro-ophthalmology (Drs. Cogan, Donaldson, Smith, and Gay) as well as brief courses on radiation ophthalmology and informal participation in various clinical and scientific conferences. The ophthalmo-neuro-medical conferences which were organized by Dr. Lawton Smith last year are being continued at monthly intervals by Dr. Donaldson.

The annual two-day conference on ophthalmic biochemistry which was begun several years ago under the sponsorship of the Laboratory with Dr. Kinoshita as chairman, continues to be of real service to those in this highly specialized branch of eye research. A grant from the Public Health Service will permit an expansion of this conference in the forthcoming year.

The Eye Pathology Department, under the direction of Dr. Taylor Smith, operates in close and mutually satisfactory association with the Howe Laboratory. Dr. Anne Morgan as Assistant Resident in Ophthalmic Pathology and Dr. Norman Byer, a Heed Fellow, have added greatly to the study and presentation of material in both the Pathology Laboratory and in the Howe Laboratory. Drs. Kuwabara and Cogan have been intimately associated with Dr. Smith in the survey of all cases that go through the Pathology Department and in the conduction of the weekly Pathology Conferences.

For the record it may be noted that Dr. Cogan's term of service on the Council of Neurologic Diseases and Blindness of the National Institutes of Health was ended this past year and Dr. Grant has been appointed to the Sensory Disease Study Section of the Institute. Dr. Grant has also been appointed to the Advisory Council of the Society to Combat Blindness.

Organization

The future of the Howe Laboratory will depend in large measure on its ability to maintain a scientific staff and physical quarters commensurate with its position of a pioneer in oph-

thalmic research. Since World War II it has coped with economic tribulations engendered by the inflation and by the natural process of growth. Whereas the budget prior to the War was derived almost entirely from income on endowment — about $30,000 annually — only about one-third of the budget is presently covered by this source. The bulk of support now comes from various agencies and individuals who by contributing sums of various dimensions have permitted a reasonable expansion of operations despite the shrunken value of endowment income.

The hope has been repeatedly expressed in these Reports that substantial increase in endowment might be forthcoming since only with guaranteed capital can we encourage investigators to make a career of ophthalmic research. It is a great satisfaction, therefore, to be able to announce that the first of such funds, the Max, Martha, and Alfred M. Stern Fund, has been established at Harvard with income to be used for ophthalmic research at the Howe Laboratory. The terms of the gift stipulate preferential interest in glaucoma and cataracts, but are wisely flexible so as to permit exploration of whatever leads appear most promising.

A proposed expansion in physical quarters announced in the last Report has been confronted with a series of unanticipated hurdles. These included the steel strike, a delay in building authorization and a serious miscalculation on the estimated costs. These difficulties should soon be resolved and we hope the additional facilities will be readied by the time of the next Report.

The Howe Laboratory exists by reason of the benefaction of several agencies and a group of loyal friends. It is with gratitude that we record the names of those who have contributed to the welfare of the Laboratory this past year. These contributions are all the more appreciated since they have not been directly solicited. They have been prompted by humanitarian motives and by a faith, which we hope to justify, that money given to the Howe Laboratory for eye research will bring valuable results.

For general expenses:

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DAVID G. COGAN, M.D.
Director

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Smith, J. L. and Cogan, D. G.: The ophthalmodynamometric posture test. Am. J. Ophth. *48*:735–740, December, 1959.

Snyder, C. J.: Examining an old wound. Conn. Med. *23*:505–508, August, 1959.

Sweebe, E. C. and Cogan, D. G.: Adenocarcinoma of the meibomian gland: A pseudo-chalazion entity. A.M.A. Arch. Ophth. *61*:282–290, February, 1959.

LECTURES

ANDREWS, J. S.

Biochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

COGAN, D. G.

Ocular effects of radiation: Ionizing electromagnetic. American Academy of Occupational Medicine, in Boston, Massachusetts, February 13, 1959.

Case Report: Lacrimal gland tumor. New England Ophthalmological Society, in Boston, Massachusetts, February 18, 1959.

The ocular fundus. Postgraduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, March 3, 1959.

Retinal dehydrogenases. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 14, 1959.

Neuro-ophthalmology. Series of lectures to Postgraduate Course in Neuro-ophthalmology, in Boston, Massachusetts, May 18–23, 1959.

Retinal dehydrogenases. American Ophthalmological Society, in Hot Springs, Virginia, May 29, 1959.

Discussion: Dr. R. S. Jampel's paper, "The representation of the near reflex of the eye on the general cortex of the macaque." Association for Research in Ophthalmology, in Atlantic City, New Jersey, June 11, 1959.

Convergence nystagmus. American Medical Association Meeting, Section on Ophthalmology, Panel on Neuro-ophthalmology, in Atlantic City, New Jersey, June 12, 1959.

Ocular complications of diabetes. Section of Diabetes, Course in Internal Medicine, Massachusetts General Hospital, in Boston, Massachusetts, July 3, 1959.

Ocular manifestations of systemic disease. House Officer Lecture, Massachusetts General Hospital, in Boston, Massachusetts, July 24, 1959.

Histochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

Radiation and the Eye. United States Naval Submarine Medical Officers' Course, in New London, Connecticut, October 9, 1959.

Neuro-ophthamology. Connecticut Postgraduate Seminar in Psychiatry and Neurology, in New Haven, Connecticut, October 14, 1959.

Visual Pathways and Neurologic Field Defects. Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, October 31 and November 3, 1959.

with Kuwabara, T. Dystrophic ophthalmoplegia externa. New England Ophthalmological Society, in Boston, Massachusetts, November 18, 1959.

Eye pathology. Mallory Institute Residents, Boston City Hospital, in Boston, Massachusetts, December 9, 1959.

Ocular pathology of systemic disease. Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, December 15, 1959.

Ophthalmic pathology. Harvard Medical School, Department of Pathology, in Boston, Massachusetts, December 19, 1959.

House Officer Lectures, Massachusetts Eye and Ear Infirmary
Fundus pathology. April 16, 1959.
Ocular pathology in systemic disease. August 6 and 11, 1959.

DONALDSON, D. D.

Manifestations of systemic disease. Eastern New York Eye Society, in Schenectady, New York, January 8, 1959.

Tumors and cysts of the conjunctiva. New England Ophthalmological Society, in Boston, Massachusetts, January 21, 1959.

Inflammatory and degenerative conditions of the conjunctiva. New England Ophthalmological Society, in Boston, Massachusetts, February 18, 1959.

Lenticular opacities associated with endocrine disorders. Endocrine Conference, Massachusetts General Hospital, in Boston, Massachusetts, March 16, 1959.

Some interesting ocular injuries. New England Ophthalmological Society, in Boston, Massachusetts, March 18, 1959.

The eyes of twins. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 14, 1959.

Industrial ophthalmology. Public Health Group, in Boston, Massachusetts, April 16 and 23, 1959.

Some interesting systemic diseases of the anterior segment of the eye. Episcopal Eye and Ear Association, in Washington, D. C., May 1, 1959.

Neuro-anatomy as related to neuro-ophthalmology. Washington Medical Center Group, in Washington, D. C., May 2 and 8, 1959.

Diseases involving the chamber and angle. Pittsburgh Ophthalmologic Society, in Pittsburgh, Pennsylvania, May 18, 1959.

Neuro-anatomy. Series of lectures to Postgraduate Course in Neuro-Ophthalmology, in Boston, Massachusetts, May 18–23, 1959.

Conditions of the angle of the anterior chamber. Postgraduate Glaucoma Course, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, June 15, 1959.

Gonioscopy as a means of diagnosis. Maine Medical Society, in Rockland, Maine, June 23, 1959.

Keratopathies and corneal dystrophies. Lancaster Course, in Waterville, Maine, July 27, 1959.

Preventable eye diseases. Regional Lions Meeting, in Fall River, Massachusetts, October 8, 1959.

Neuro-anatomy and anterior segment pathology. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 29—October 16, 1959

House Officer Lectures, Massachusetts Eye and Ear Infirmary

Diseases of the angle of the anterior chamber, January 6, 1959.

Congenital cataracts. February 26, 1959.

Developmental cataracts. March 5, 1959.

Tumors of the iris. June 30, 1959.

Systemic diseases of the eye. November 19 and December 3, 1959.

FUTTERMAN, S.

Biochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

GAY, A. J.

Neuro-ophthalmology. Series of lectures to Postgraduate Course in Neuro-ophthalmology, in Boston, Massachusetts, May 18–23, 1959.

GRANT, W. M.

Participation in Josiah Macy Jr. Foundation Conference Program, Fourth Symposium on Glaucoma, in Princeton, New Jersey, March 8–10, 1959.

Progress report on aqueous outflow. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 14, 1959.

Discussion: Retinal dehydrogenases. David G. Cogan. American Ophthalmological Society, in Hot Springs, Virginia, May 29, 1959.

Postgraduate Glaucoma Course, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, June 15, 17 and 18, 1959:

Ocular hydrodynamics.

Gonioanatomy.

Aplanation tonometry.

Pathology of glaucoma.

Research in glaucoma.

Toxicology, tonometry and tonography. Series of lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine, July 27 and 28, 1959.

Participation in Glaucoma Symposium of National Society for Prevention of Blindness, in Chicago, Illinois, October 10, 1959.

Toxicology. Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, October 20, 1959.

Pharmacology of the eye. Harvard Medical School, Department of Pharmacology, in Boston, Massachusetts, December 19, 1959.

House Office Lectures, Massachusetts Eye and Ear Infirmary:

Aplanation tonometry, July 9, 1959.

Secondary glaucoma. November 17, 1959.

KERN, H. L.

Biochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

KINOSHITA, J. H.

Interaction of the dehydrogenases of the shunt mechanism with lactic dehydrogenase in ocular tissues. Fourth Conference on Ophthalmic Biochemistry, in Cambridge, Massachusetts, February 21 and 22, 1959.

Biochemistry of the lens and cornea. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

KUPFER, C.

Electrophysiology. Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, January 12 and 14, 1959.

Macula function. House Officer Lecture, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, June 16, 1959.

Physiology of the eye. Series of lectures and laboratory exercises, Harvard Medical School, Department of Physiology, in Boston, Massachusetts, May 31-April 3, 1959.

Aqueous dynamics. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, December 2, 3 and 5, 1959.

KUWABARA, T.

Histochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

with Cogan, D. G. Dystrophic ophthalmoplegia externa. New England Ophthalmological Society, in Boston, Massachusetts, November 18, 1959.

MEROLA, L. O.

Biochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

SMITH, J. L.

The usefulness of retinal arterial pressure measurements. New England Cardiovascular Society, in Boston, Massachusetts, February 9, 1959.

The effects of posture on the ophthalmodynamometric diagnosis of carotid insufficiency. Wilmer Meeting, Johns Hopkins Hospital, in Baltimore, Maryland, March 20, 1959.

Neuro-ophthalmology Conference. New England Ophthalmological Society, in Boston, Massachusetts, April 13, 1959.

Neuro-ophthalmology. Series of Lectures to Postgraduate Course in Neuro-ophthalmology, in Boston, Massachusetts, May 17–23, 1959.

SNYDER, C. J.

Examining an old wound. New England Ophthalmological Society, in Boston, Massachusetts, January 21, 1959.

T. R. New England Ophthalmological Society, in Boston, Massachusetts, April 13, 1959.

SPECTOR, A.

Biochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 30-October 17, 1959.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology.....Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.